DRUG NAME: Sacituzumab govitecan

SYNONYM(S):

COMMON TRADE NAME(S): TRODELVY® (USA)

CLASSIFICATION: miscellaneous

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Sacituzumab govitecan is an antibody-drug conjugate (ADC) comprised of a humanized IgG1κ monoclonal antibody linked to a small molecule topoisomerase inhibitor (SN-38) by a hydrolysable linker. Sacituzumab is an inhibitor of trophoblast cell-surface antigen 2 (Trop-2), a protein that is associated with regulating cancer cell proliferation, migration, invasion, and metastasis and is overexpressed in many solid epithelial cancers. Sacituzumab binds to Trop-2 on the tumour cell surface and is internalized, which releases SN-38 both intracellularly and within the tumour microenvironment, leading to DNA damage, apoptosis, and cell death.[1-3]

USES:

Primary uses:

Breast cancer[2]

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Contraindications:

- history of hypersensitivity reaction to sacituzumab govitecan or sacituzumab or irinotecan[1]

Caution:

- severe ***neutropenia and febrile neutropenia*** are reported[1]
- patients who are ***homozygous for UGUT1A1*28 allele*** (uridine diphosphate-glucuronosyl transferase 1A1) are at increased risk of neutropenia and other adverse reactions[1]
- severe ***diarrhea*** is reported and can be managed with prompt use of loperamide[1]
- an excessive ***cholinergic response*** (e.g., abdominal cramping, diarrhea, salivation) may be exhibited; premedication with atropine may be required[1]
- severe and life-threatening ***hypersensitivity*** reactions within 24 h of dosing are reported; premedication and close observation is recommended[1]
- ***teratogenicity*** and/or ***embryo-fetal lethality*** is possible if administered to a pregnant woman; contraception is recommended for female patients and male patients with female partners of reproductive potential[1]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials.

Developed: 15 March 2021
Revised: 1 May 2021

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	***anemia*** (52%, severe 12%)
	febrile neutropenia (6%)
	neutropenia (54-64%, severe 11-43%); risk of severe reactions may be increased in patients homozygous for UGT1A1*28 allele
	thrombocytopenia (14%, severe 3%)
gastrointestinal	*emetogenic potential:* moderate[4]
	abdominal pain (26%, severe 1%)
	constipation (34%, severe 1%)
	diarrhea (62-63%, severe 9%)
	mucositis (14%, severe 1%)
	nausea (69%, severe 5-6%)
	vomiting (45-49%, severe 4-6%)
general disorders and administration site conditions	*extravasation hazard:* none[5]
	edema (19%)
	fatigue (57%, severe 8%)
	pyrexia (14%)
immune system	***hypersensitivity*** (37%, severe 1%);
infections and infestations	***respiratory infection*** (26%, severe 3%)
	urinary tract infection (21%, severe 3%)
investigations	***alkaline phosphatase increase*** (57%, severe 2%)
	ALT increase (35%, severe 2%)
	AST increase (45%, severe 3%)
	hyperglycemia (24%, severe 4%)
	hypokalemia (19%, severe 2%)
	hypomagnesemia (21%, severe 1%)
	hypophosphatemia (16%, severe 9%)
metabolism and nutrition	appetite decrease (30%, severe 1%)
	dehydration (13%, severe 5%)
musculoskeletal and connective tissue	arthralgia (17%)
	back pain (23%)
	extremity pain (11%)
nervous system	dizziness (22%)
	dysgeusia (11%)
	headache (23%, severe 1%)
	neuropathy (24%)

Developed: 15 March 2021
Revised: 1 May 2021

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
psychiatric	insomnia (13%)
respiratory, thoracic and mediastinal	cough (22%)
	dyspnea (21%, severe 3%)
skin and subcutaneous tissue	***alopecia*** (38%)
	dry skin (15%)
	pruritus (17%)
	rash (31%, severe 3%)

Adapted from standard reference[1] unless specified otherwise.

INTERACTIONS:

Concomitant administration with ***UGT1A1 inhibitors or inducers*** may affect the systemic exposure to SN-38 and should be avoided if possible. UGT1A1 ***inhibitors*** may increase the incidence of adverse reactions due to increased exposure to SN-38. UGT1A1 ***inducers*** may substantially reduce the systemic exposure to SN-38, possibly affecting treatment outcome.[1]

SUPPLY AND STORAGE:

Injection: Immunomedics, Inc. supplies sacituzumab govitecan as180 mg vials of lyophilized powder. Refrigerate. Protect from light.[1]

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Additional information:
- Protect infusion bag from light during storage and administration.[1]

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous[1]	do NOT use
Intermittent infusion[1]	***initial infusion: over 3 h***; ***subsequent infusions: over 1-2 h*** if prior infusions are tolerated

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BC Cancer administration guideline noted in ***bold***, ***italics***

Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

BC Cancer usual dose noted in ***bold, italics***

	Cycle Length:	
Intravenous:	3 weeks[1]:	***10 mg/kg*** (range 5-10 mg/kg) ***IV for one dose on days 1 and 8*** (total dose per cycle 20 mg/kg [range 10-20 mg/kg])

REFERENCES:

1. Immunomedics Inc. TRODELVY® full prescribing information. Morris Plains, New Jersey, USA; Apr 2020.
2. Lexi-Drugs® - Lexicomp Online (database on the Internet). Sacituzumab govitecan. Wolters Kluwer Clinical Drug Information Inc., 29 January 2021. Available at: http://online.lexi.com. Accessed 12 March 2021.
3. Goldenberg DM, Stein R, Sharkey RM. The emergence of trophoblast cell-surface antigen 2 (TROP-2) as a novel cancer target. Oncotarget 2018;9(48):28929-29006.
4. BC Cancer. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; 1 July 2020.
5. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; January 2016.

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